International Patent Application
No. PCT/EP2004/010582
BioNetWorks GmbH
29607P WO/MDmh

New Claims

1. Use of an 11-β-HSD-type 1 and/or type 2 inhibitor or a pharmaceutically acceptable salt thereof, for the manufacture of a pharmaceutical agent for the prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage, wherein said use is for the prevention and/or treatment of osteoporosis, postmenopausal osteoporosis, lytic bone metastases, arthritis, juvenile chronic arthritis and/or adjuvant arthritis, infectious diseases, bone loss by cancer, bone loss by HIV, tooth loss, bone marrow inflammation, synovial inflammation, cartilage and/or bone erosion and/or proteoglycan damage.

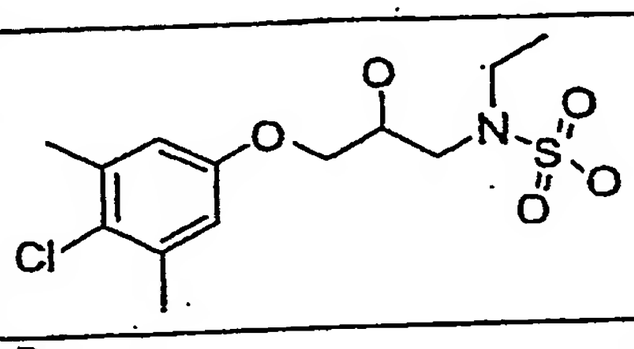
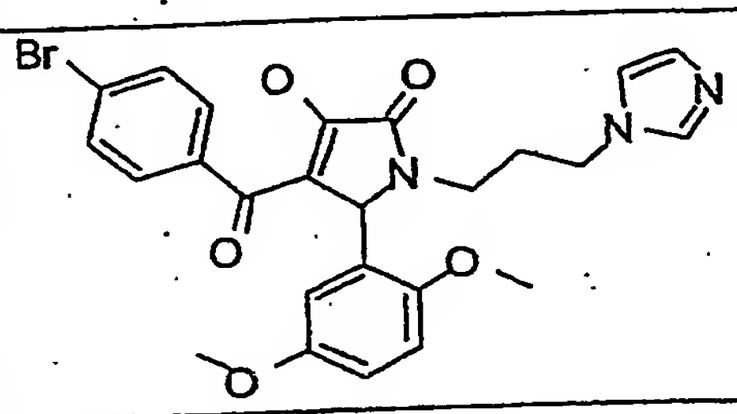
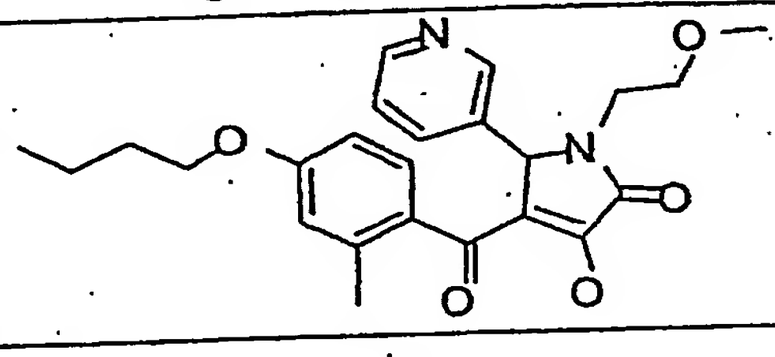
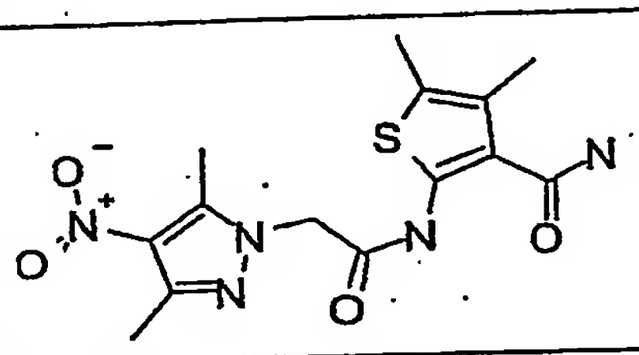
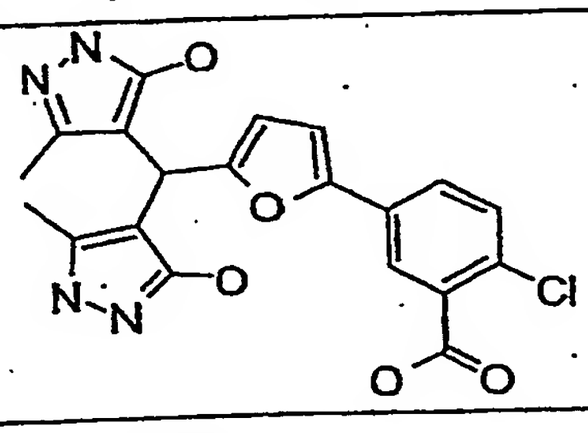
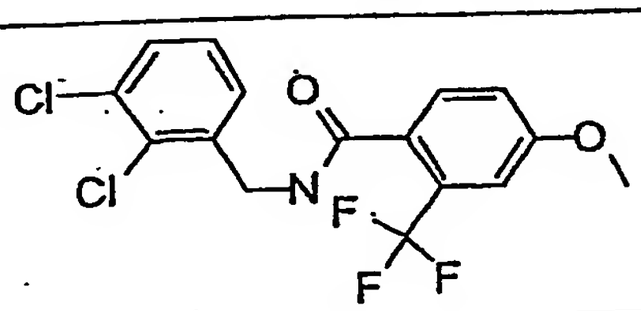
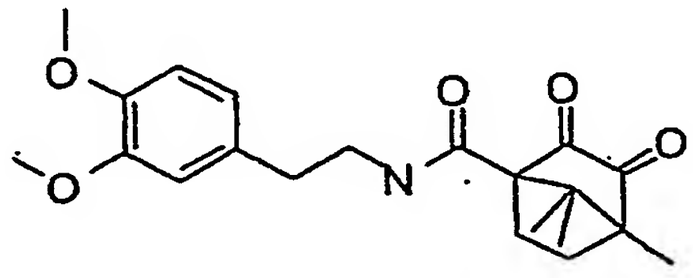
2. The use according to claim 1 for the prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage in a mammal.

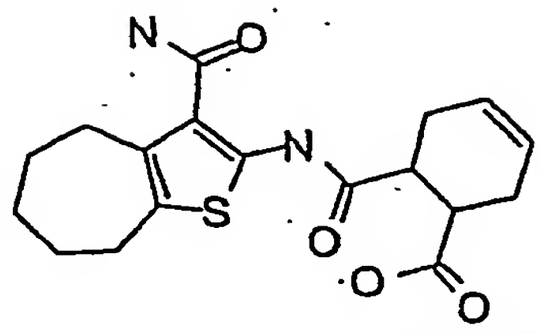
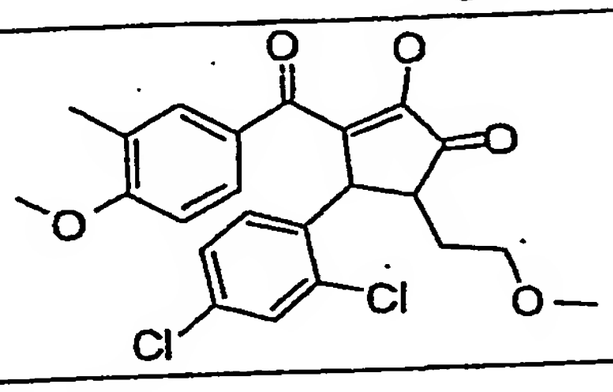
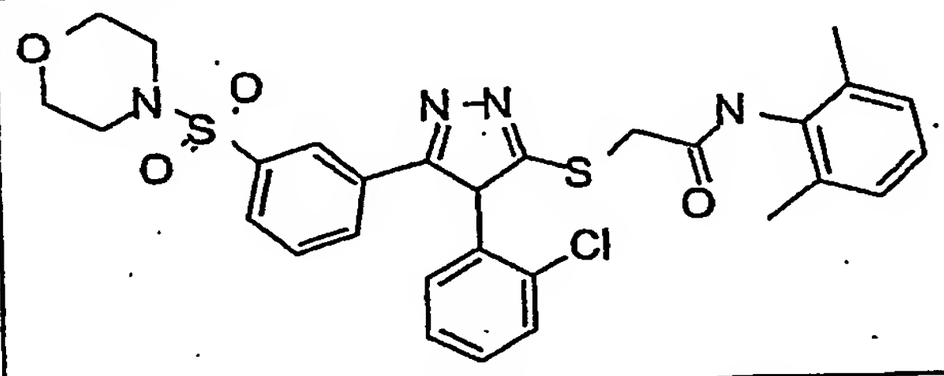
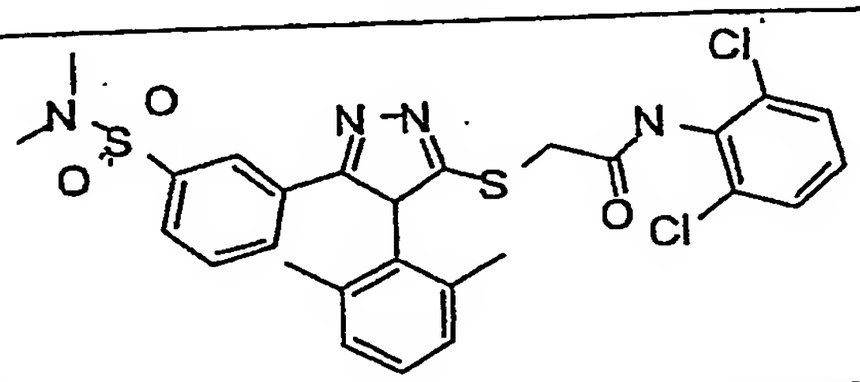
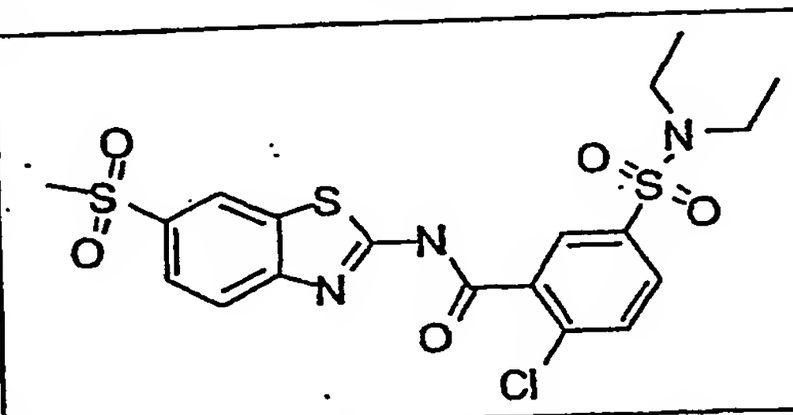
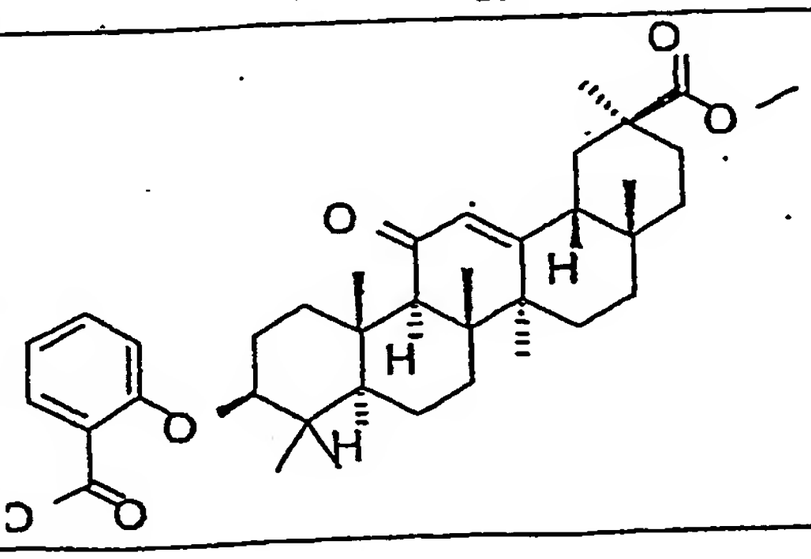
3. The use according to claim 2, wherein the mammal is a human.

4. The use according to claim 1, wherein said use is for the prevention and/or treatment of periodontitis and/or arthritis selected from the group consisting of osteoarthritis and/or rheumatoid arthritis.

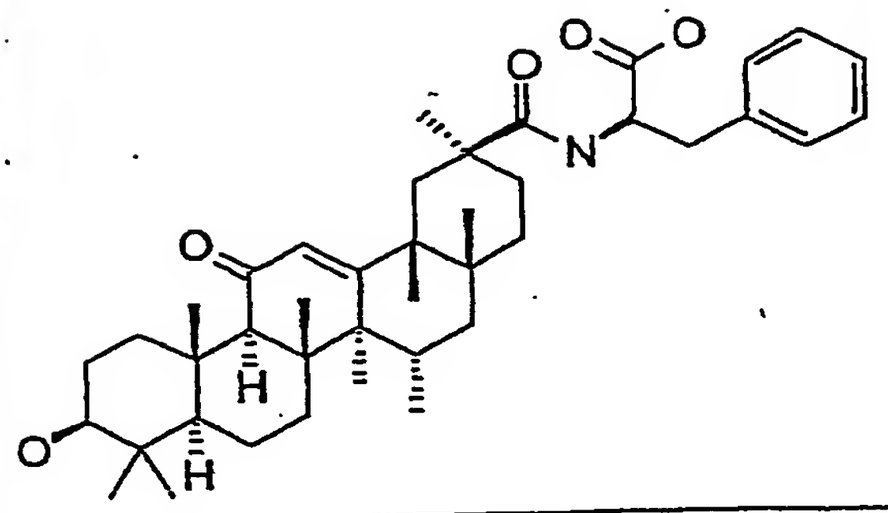
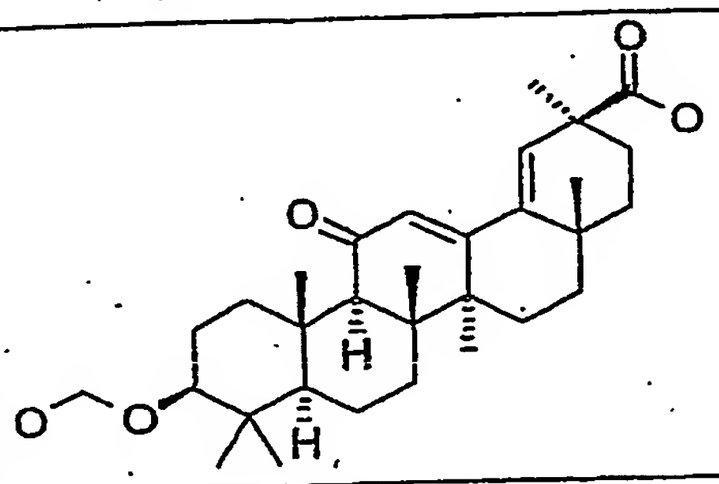
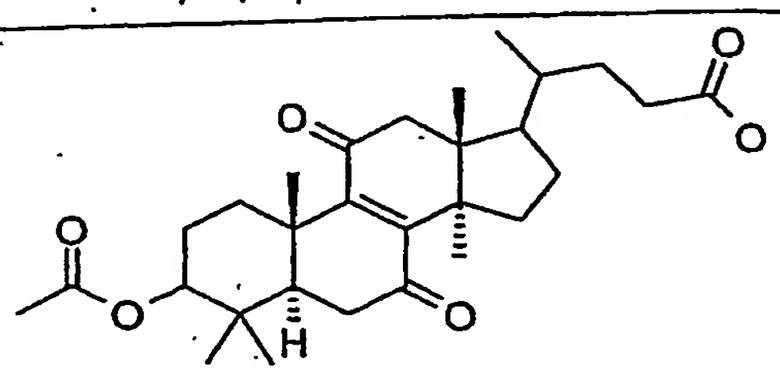
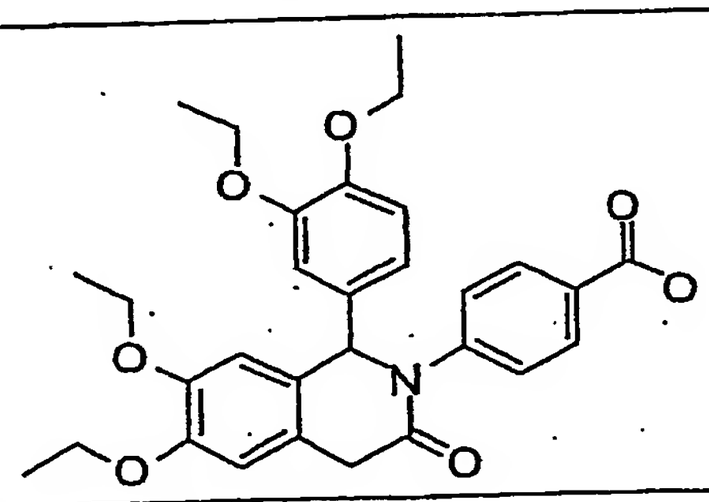
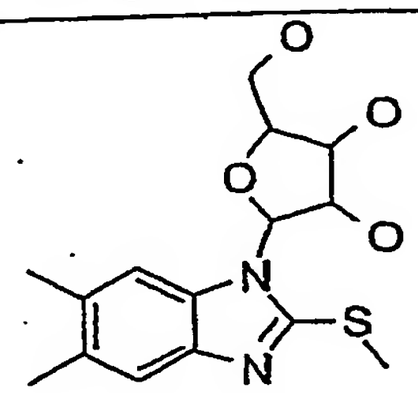
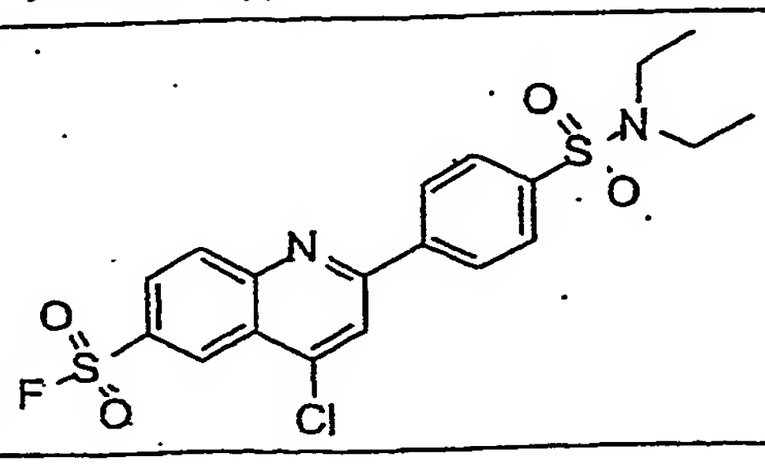
5. The use according to any one of claims 1 to 4, wherein the 11- β-HSD-type 1 and/or type 2 inhibitor is 18-β-glycyrrhetinic acid.

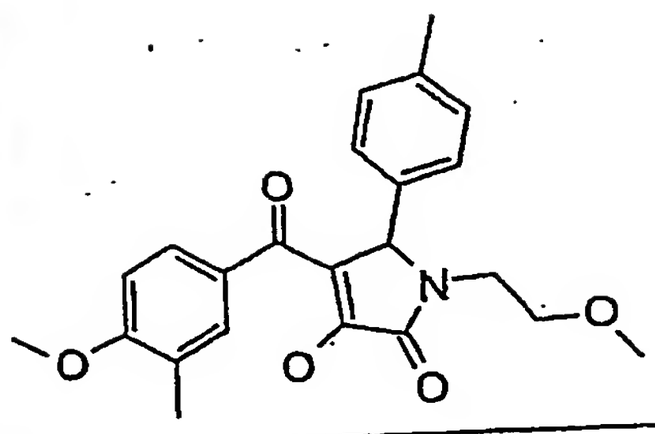
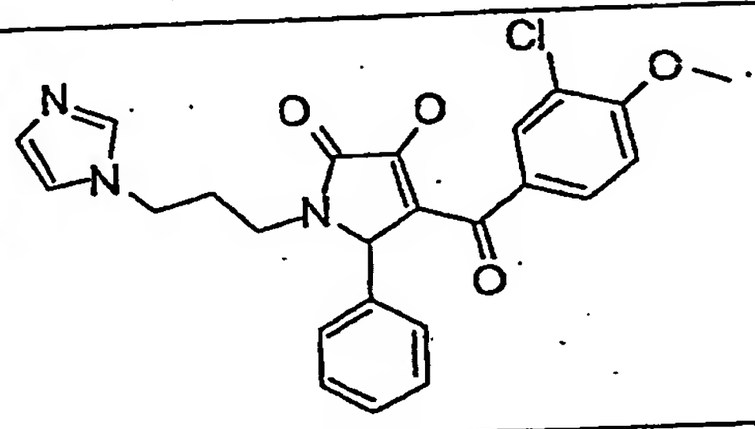
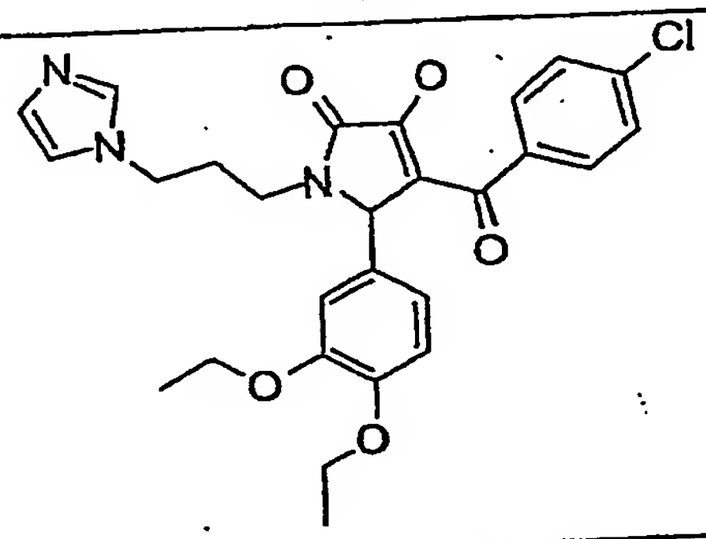
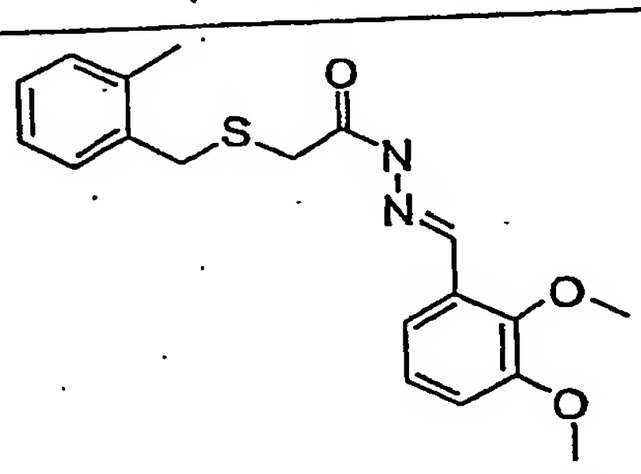
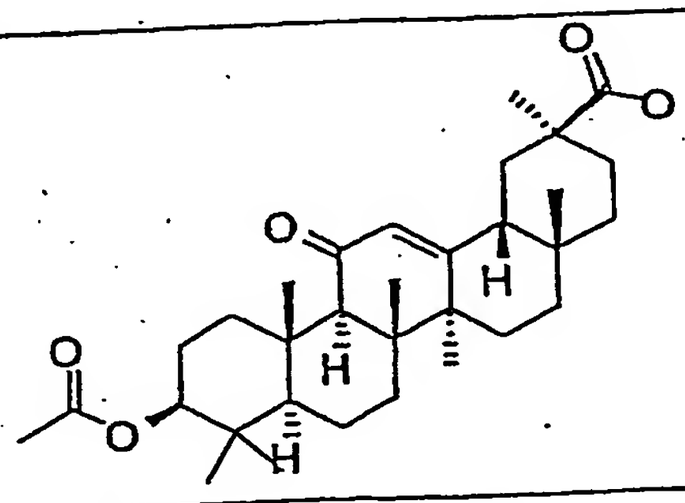
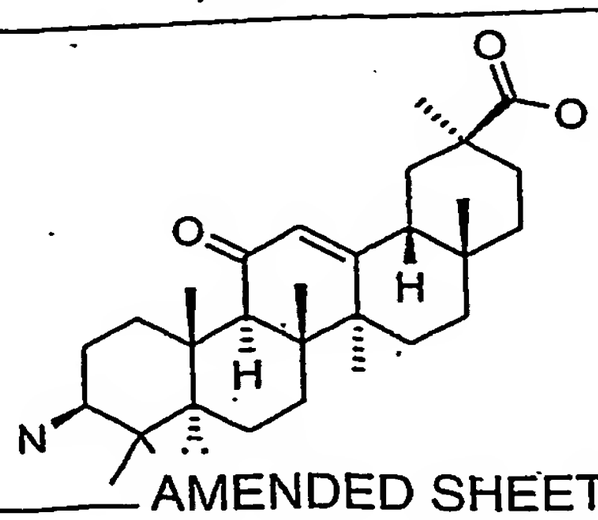
6. The use according to any one of claims 1 to 4, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the following formulas:

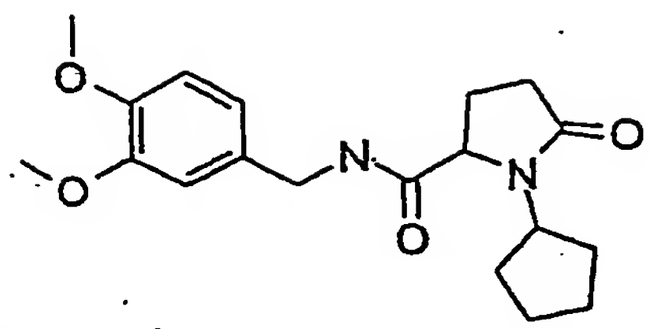
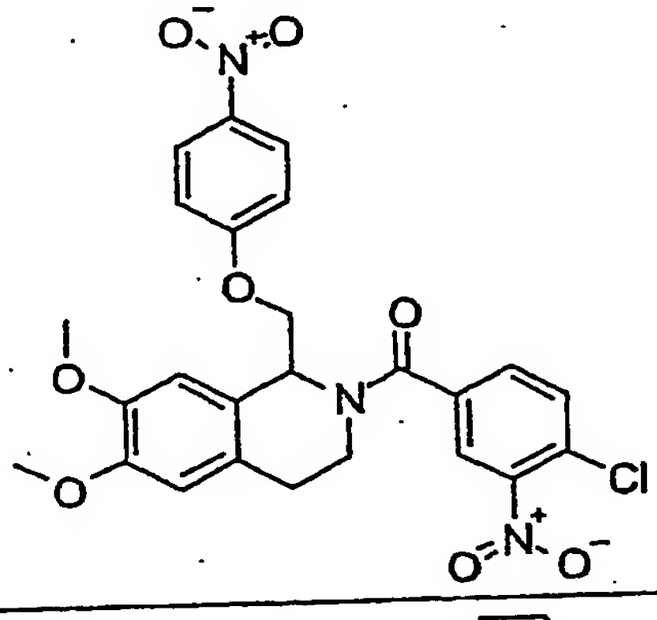
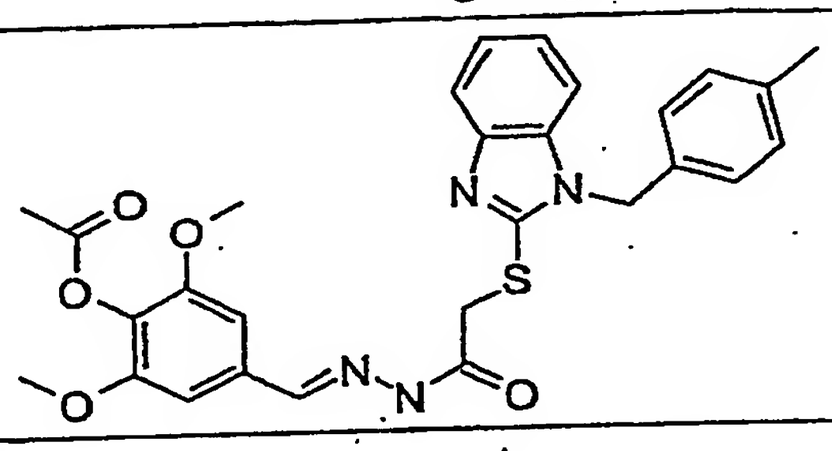
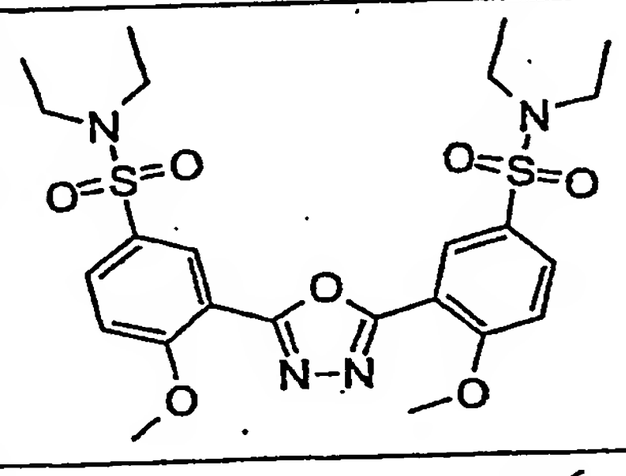
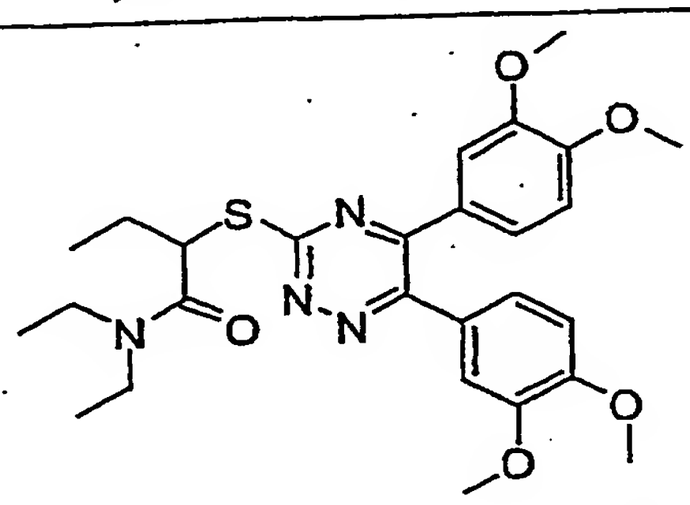
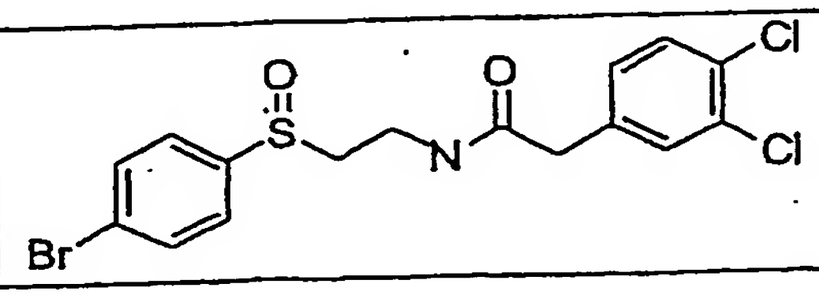
Compound Name	Structure
Formula 1	
Formula 2	
Formula 3	
Formula 4	
Formula 5	
Formula 6	
Formula 7	

Formula 8	
Formula 9	
Formula 10	
Formula 11	
Formula 12	
Formula 13	

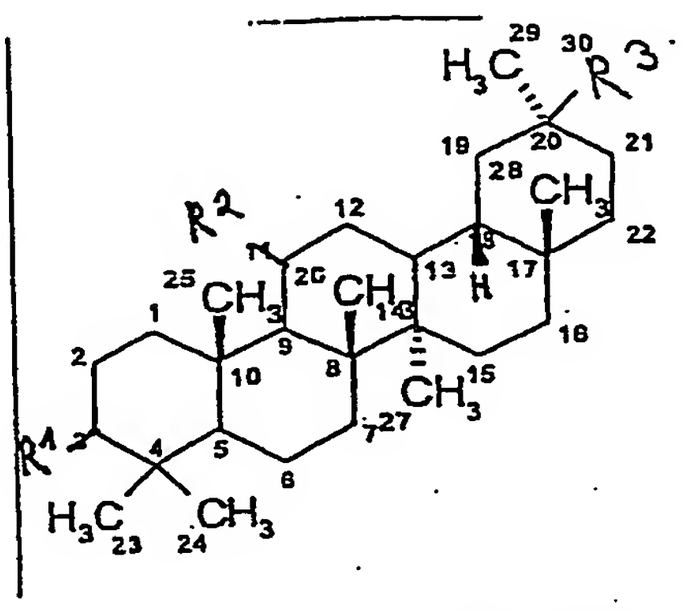
AMENDED SHEET

Formula 14	
Formula 15	
Formula 16	
Formula 17	
Formula 18	
Formula 19	

Formula 20	
Formula 21	
Formula 22	
Formula 23	
Formula 24	
Formula 25	

Formula 26	
Formula 27	
Formula 28	
Formula 29	
Formula 30	
Formula 31	

7. The use according to any one of claims 1-4, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor has the structure of formula I:



formula I

wherein R^1 is

a hydrogen,

a linear or branched C_1-C_{10} alkyl group,

a linear or branched C_1-C_{10} alkenyl group,

a linear or branched C_1-C_{10} alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-aminoalkyl) or thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group,

wherein said cyclic group may be mono- or polysubstituted with an ester, amino, halo, hydroxy, C_1-C_4 alkoxy, carboxy, carbonyl, C_1-C_4 alkoxycarbonyl, carboxyphenoxy, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)amino, sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-alkyl), thio, C_1-C_4 alkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl group;

R^2 is

a hydrogen, C_1-C_4 alkyl, carbonyl, ester, amino, halo, carbonyl, hydroxy, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)

amino, carboxy-di(C_1-C_4-alkyl), sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-alkyl) or thio group;

R^3 is

a hydrogen,

a linear or branched C_1-C_{10} alkyl group,

a linear or branched C_1-C_{10} alkenyl group,

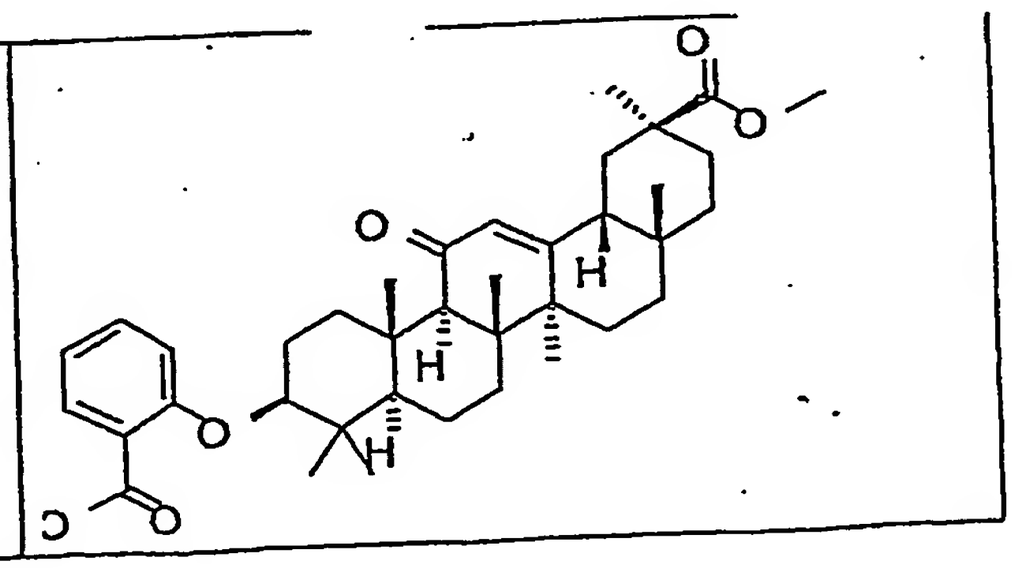
a linear or branched C_1-C_{10} alkynyl group,

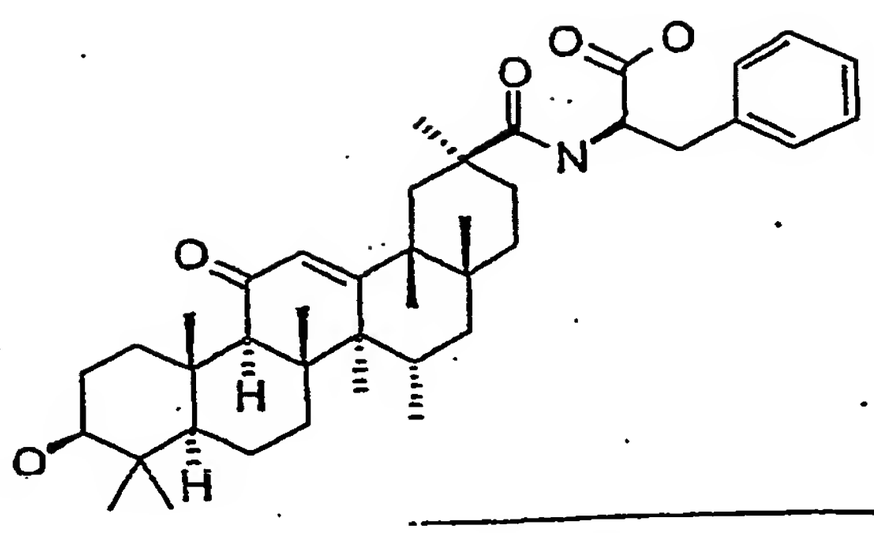
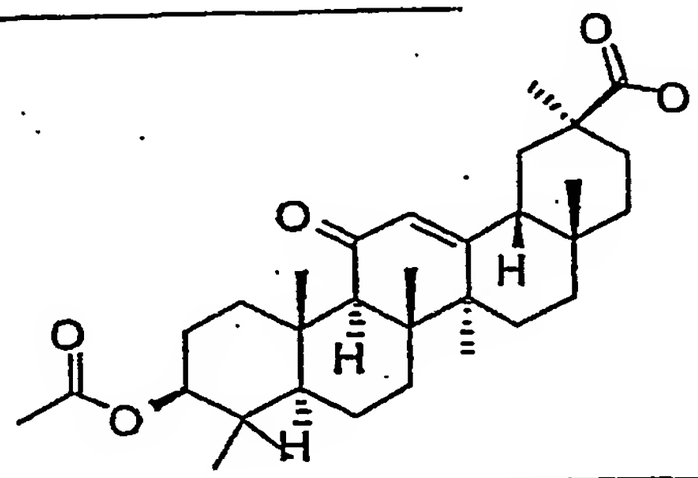
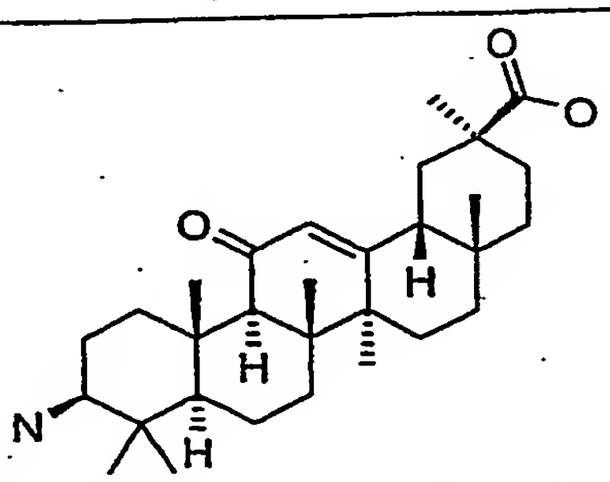
an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-aminoalkyl) or thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group;

wherein the chemical bond from carbon 13 to 14 is saturated or unsaturated;
or a salt or derivative thereof in the form of an individual enantiomer, diastereomer or a mixture thereof.

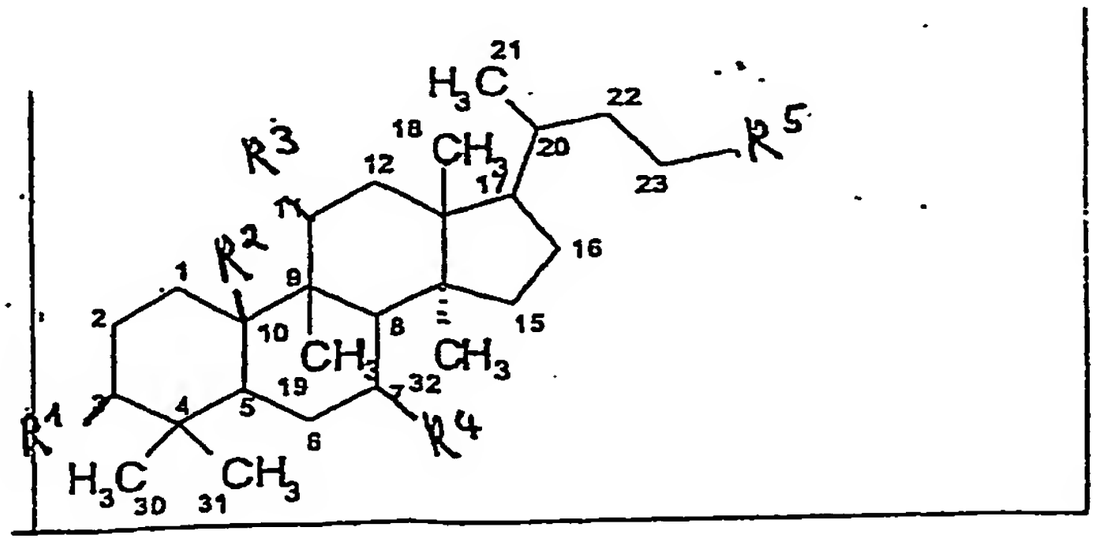
8. The use according to claim 1, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is selected from the group consisting of the following formulas:

Formula 13



Formula 14	
Formula 24	
Formula 25	

9. The use according to any one of claims 1-4, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor has the structure of formula II:



formula II

wherein R^1 is

a hydrogen,

a linear or branched C_1-C_{10} alkyl group,

a linear or branched C_1-C_{10} alkenyl group,

a linear or branched C_1-C_{10} alkynyl group,

an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-aminoalkyl), thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group,

wherein said cyclic group may be mono- or polysubstituted with an ester, amino, halo, hydroxy, C_1-C_4 alkoxy, carbonyl, carboxy, C_1-C_4 alkoxycarbonyl, carboxyphenoxy, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)amino, sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-alkyl), thio, C_1-C_4 alkyl, C_2-C_4 alkenyl or C_2-C_4 alkynyl group;

R^2 is a hydrogen or C_1-C_4 alkyl,

R^3 and R^4 are each selected from

a hydrogen

a linear or branched C_1-C_{10} alkyl group,

a linear or branched C_1-C_{10} alkenyl group,

a linear or branched C_1-C_{10} alkynyl group,

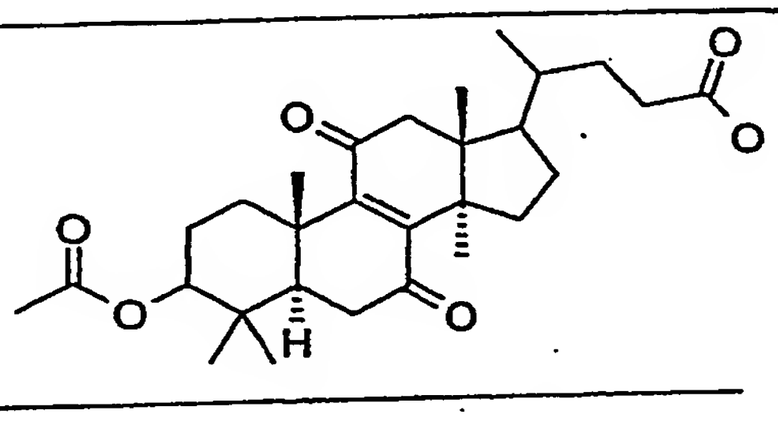
an ester, amino, halo, hydroxy, carbonyl, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl)amino, carboxy-di(C_1-C_4-alkyl)sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-C_4-alkyl), sulfono (C_1-C_4-aminoalkyl), thio group, a saturated or unsaturated, aromatic or heteroaromatic mono- or polycyclic group;

R^5 is a hydrogen, C_1-C_4 alky, carbonyl, ester, amino, halo, hydroxy, carboxy, carboxyphenoxy, C_1-C_4 alkoxy, C_1-C_4 alkoxy carbonyl, C_1-C_4 alkyl amino, di-(C_1-C_4-alkyl)amino, cyano, carboxy amide, carboxy-(C_1-C_4-alkyl) amino, carboxy-di(C_1-C_4-alkyl), sulfo, sulfido (C_1-C_4-alkyl), sulfoxido (C_1-

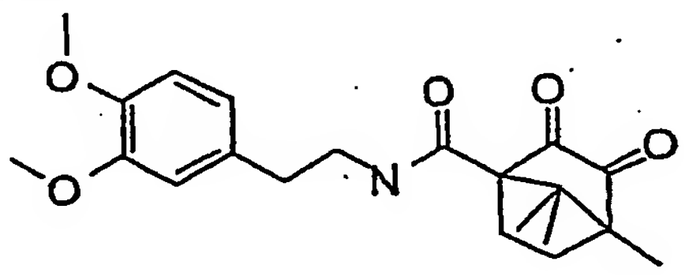
C_4-alkyl), sulfono (C_1-C_4-alkyl) or thio group,

wherein the chemical bond from carbon 8 to 9 is saturated or unsaturated;
wherein the chemical bond from carbon 13 to 14 is saturated or unsaturated;
or a salt or derivative thereof in the form of an individual enantiomer, diastereomer or a mixture thereof.

10. The use according to claim 1, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is:

Formula 16	

11. The use according to claim 6, wherein the 11-β-HSD-type 1 and/or type 2 inhibitor is:

Formula 7	

12. The use of any one of claims 1 to 11, wherein the pharmaceutical agent comprises at least one 11-β-HSD-type 1 and/or type 2 inhibitor in combination with at least one active ingredient being effective in the

prevention and/or treatment of inflammation-induced and/or immune-mediated loss of bone and/or cartilage.

13. The use according to any one of claims 1 to 12, wherein the pharmaceutical agent is administered in a dose of 5 to 100 mg/kg body weight per day.

14. The use of any one of claims 1 to 13, wherein the pharmaceutical agent is administered orally, sublingually, intravenously, intramuscularly, intraarticularly, intraarterially, intramedullarily, intrathecally, intraventricularly, intraocularly, intracerebrally, intracranially, respiratorally, intratracheally, nasopharyngeally, transdermally, intradermally, subcutaneously, intraperitoneally, intranasally, enterally, topically, via rectal means, via infusion and/or via implant.

15. The use according to claim 14, wherein the pharmaceutical agent is administed orally.